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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/909,460	07/18/2001	Lynn B. Lunsford	08191-014002	1198

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FISH & RICHARDSON PC
P.O. BOX 1022
MINNEAPOLIS, MN 55440-1022

EXAMINER	
MARVICH, MARIA	
ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
09/14/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	09/909,460	LUNSFORD ET AL.	
	Examiner	Art Unit	
	MARIA B. MARVICH	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6/30/10*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,52,64-69 and 85-113* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4, 52, 64-69 and 85-113* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 October 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to an amendment filed 6/30/10. Claims 1, 4, 52, 64-69 and 85-113 are pending in the application.

In the office action mailed 5/01/09, it was set forth that support for the limitation that a microparticle comprises in addition to a polymeric matrix and a nucleic acid, a lipid is found in the priority document PCT/US98/01499 filed 1/22/1998. PCT/US98/01499 teaches microparticles for delivery of nucleic acids wherein the particles comprise a polymeric matrix, nucleic acid and a stabilizing compound. This stabilizing compound can be a lipid such as CTAB and furthermore interacts with the nucleic acids of the particles. Therefore, PCT/US98/01499 supports the teachings of the instant specification and the instant claims. Therefore, the instant claims are afforded the priority date of PCT/US98/01499, 1/22/1998.

Applicants' arguments are persuasive regarding the objections to claims 66 and 96.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4, 85, 88, 90-93, 95-100, 102 and 103 are rejected under 35 U.S.C. 102(b) as being anticipated by McElligott et al (WO 94/23738; see entire document). **This rejection is maintained for reasons of record in the office action mailed 12/30/09 and restated below.**

McElligott et al teaches construction of microparticles of 1-250 microns wherein the microparticles comprise a polymeric matrix such as polycaprolactone or copolymers of lactic and glycolic acid encapsulating nucleic acid (see e.g. abstract, page 6, line 1-5, page 42, figure 2 and page 30, line 1-10) wherein the complex can further comprise lipid (see e.g. page 49, , claim 7). According to the specification such polymers have a solubility of less than about 1 mg/L. The nucleic acid is intended for expression and hence comprises expression control sequences, as well as sequences for immunization i.e. HIV (see page 12, line 13-23 and page 29, line 15-35). Example 1 teaches use of plasmid DNA that was no so treated to believe that it is less than 100% supercoiled. Targeting molecules are included (see e.g. page 7-27)

Response to Arguments

Applicants have presented evidence that microparticles produced by the method of double emulsion techniques result in DNA that is less than 39% supercoiled. While this evidence is convincing, a more thorough reading of Ando et al suggests that the method of McElligot et al may not be the same as that of Ando.

> One of the most common techniques for preparation of biodegradable polymer microspheres encapsulating hydrophilic molecules is the double-emulsion solvent-evaporation method. Using this technique, the molecule to be encapsulated is placed in aqueous solution while the polymer is dissolved in an organic phase commonly consisting of methylene chloride or ethyl acetate. The two phases (volume organic/volume aqueous) 3-20) are emulsified, typically by sonication or homogenization. This primary emulsion is then added to a second aqueous phase (20- to 100-fold larger volume) and again mixed by homogenization to form the (water-in-oil)-in-water double emulsion. Upon evaporation of the partially water-miscible solvent, the

> polymer-containing droplets harden to form microspheres which can then be isolated by filtration or centrifugation. Lyophilization removes water from the interior aqueous phase resulting in a dry suspension of the encapsulated material within the polymer matrix.

In other words, the methods require water-in-oil-in water method wherein the DNA is mixed in water, the polymer is mixed in organic polymer and then the combination is mixed with water. However, McElligot et al teach

> "For microencapsulation plasmid pMH-40 DNA [500 ug or 2000 ug in 500 uL 10 mM tris (pH7.4), 1 mM EDTA (TE) buffer] or plasmid pRC/CMV/Bgal DNA [500 ug in 500 ul 10 mM tris (pH 7.4), 1 mM EDTA (TE) buffer] plus 500 ul of 50 mg/mL Herring sperm DNA (Boehringer Mannheim, Indianapolis, IN) dissolved in TE was incubated in a shaking water bath at 65°C for 30 min to promote mixing. The biodegradable polymer used for encapsulation contained the monomers lactide and glycolide in a ratio of 65:35 (dI-PLGA) (Medisorb Technologies Int., Cincinnati, OH) was weighed into a 50 mL glass screw-cap tube and dissolved in 31.7 g of ethyl acetate. To this was added, 0.75 g of M-17 tungsten microcarrier particles (Biorad, Richmond, CA), the contents were vigorously agitated and then poured into a 300 mL water jacketed reaction vessel cooled to 0°C. An additional 43.7 g of ethyl acetate was added to the reactor and the mixture was probe sonicated (Tekmar Model TM375) as 1 mL of DNA solution was slowly added using a Icc syringe and 18 gauge needle. After 30 sec of sonication, 74 g of 360 fluid 1000 cs silicon oil (Dow Corning, Ithaca, NY) was added to the reactor over 2 min and this mixture was then immediately quenched by stirring at room temperature in 2.5 liters of heptane (Chempure M138 KBJS) . After 3.5 h the solid material was collected on a 0.2 ~m filter, washed with heptane and dried in a vacuum oven for at least 3 d. These microspheres are extremely sensitive to moisture and to temperatures above 30°C and are therefore stored desiccated at 4°C".

This method teaches a water-in oil-in-oil method wherein the DNA is mixed in water, the polymer is mixed in organic polymer and then the combination is mixed with organic polymer, which is distinct from that above absent evidence to the contrary. Hence, the appendix filed is not sufficient absent evidence to the contrary to overcome the rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 4, 52, 64-69 and 85-113 are rejected under 35 U.S.C. 103(a) as being unpatentable over McElligott et al (WO94/23738; see entire document) or Hedley et al (US Patent 5,783,567; see entire document) in view of Balland et al (NATO ASI Series, 1996, Vol 290, pages 131-142; see entire document). **This rejection is maintained for reasons of record in the office action mailed 12/1/08 and 6/2/09 and 12/30/09 and restated below.**

The instant claims are drawn to a micro particle less than 20 microns in diameter comprising a polymeric matrix, a lipid and a nucleic acid wherein the polymeric matrix has a solubility in water of at less then 1 mg/l and wherein at least 50% if the nucleic acids are supercoiled.

Hedley et al teach a microparticle as well as preparations of microparticles wherein the microparticles comprise a polymeric matrix and a nucleic acid expression vector. The polymeric matrix includes one or more synthetic polymers having a solubility of less then 1 mg/l that can be biodegradable. In certain cases, the polymeric matrix can be made of a single synthetic, biodegradable copolymer, e.g., poly-lactic-co-glycolic acid (PLGA). The ratio of lactic acid to glycolic acid in the copolymer can be within the range of about 1:2 to about 4:1 by weight, preferably within the range of about 1:1 to about 2:1 by weight, and most preferably about 65:35 by weight. In some cases, the polymeric matrix also includes a targeting molecule such as a

ligand, receptor, or antibody, to increase the specificity of the microparticle for a given cell type or tissue type. The microparticles are at least 11 microns and the nucleic acid at least 80% supercoiled (see e.g. col 1-2). The nucleic acid include an expression control sequence operatively linked to an expression predict encoding at least 7 amino acids having a sequence essentially identical to the sequence of either a fragment of a naturally-occurring mammalian protein or a fragment of a naturally-occurring protein from an agent which infects or otherwise harms a mammal; or a peptide having a length and sequence which permit it to bind to an MHC class I or II molecule (col 2, line 21-36).

Balland et al teach a microparticle less than 20 microns in diameter (see e.g. page 132, paragraph 4) comprising a polymeric matrix, a lipid and a nucleic acid (see e.g. page 132, paragraph 4- 5) and preparations of these microparticles (see e.g. page 133, paragraph 4).
As an initial point, KSR forecloses the argument that a specific teaching, suggestion or motivation is required to support a finding of obviousness. See the recent Board decision Exparte Smith --USPD2d--., slip op. at 20, (BD. Pat. App. & Interfer. June 25, 2007). In this case each of Headley et al, McElligott et al and Balland et al teach design of microparticles that are less then 20 microns, as well as 11 microns. Each teaches that complexes of polymeric matrices and nucleic acids can be used to delivery the nucleic acids to cells. Headley et al and McElligott et al teach that the polymeric matrix is preferably one that has a solubility of less then 1mg/l as in the recited claims. Specifically, Headley et al and McElligott et al teach use of PLGA. Balland do not explicitly teach that the polymers have a solubility of less then 1mg/L however, these references do teach that it was known in the art to include lipids in the preparation. It would have been obvious to one of ordinary skill in the art at the time the invention was made to

include the lipid which functions as an ion pairing agent with the phosphate groups of the nucleic acids. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Response to Amendment

Applicants' argue that a statement concerning common ownership was provided and that the

> "MPEP 706.02(1)(2) also states that "Applicants may, but are not required to, submit further evidence, such as assignment records, affidavits or declarations by the common owner, or court decisions, in addition to the above-mentioned statement concerning common ownership" (emphasis in original). Consistent with the MPEP's instruction, the Statement merely referred to the recorded assignments for Application serial number 09/909,460 and U.S. Patent No. 5,783,567 in addition to containing the required statement of common ownership."

However, despite the fact that applicants must provide further evidence as the evidence of record suggests that 09/909,460 and U.S. Patent No. 5,783,567 were in fact not commonly owned at the time of invention of 09/909460, the US patent cannot be disqualified as art under common ownership. To sum up the issues, the instant claims have been rejected under 35 USC 103(a) as being obvious over the combination of over McElligott et al (Wo94/23738) or Hedley et al (US Patent 5,783,567) in view of Balland et al (NATO ASI Series, 1996, Vol 290, pages 131-142) in view of Knepp et al (US 6,264,990).

> A patent applicant or patentee urging that subject matter is disqualified has the burden of establishing that the prior art is disqualified under 35 U.S.C. 103(c). Absent proper evidence of disqualification, the appropriate rejection under 35 U.S.C. 103(a) with applying prior art under 35 U.S.C. 102(e), (f), or (g) should be made. (706.02(l))

As regards common ownership in order to disqualify art, the relevant MPEP teachings are found in 706.02(a)

> Even if the reference is prior art under 35 U.S.C. 102(e), the examiner should still consider 35 U.S.C. 102(a) for two reasons. First, if the reference is a U.S. patent or patent application publication of, or claims benefit of, an international application, the publication of the international application under PCT Article 21(2) may be the earliest prior art date under 35 U.S.C. 102(a) for the disclosure. Second, references that are only prior art under 35 U.S.C. 102(e), (f), or (g) and applied in a rejection under 35 U.S.C. 103(a) are subject to being disqualified under 35 U.S.C. 103(c) if the reference and the application were commonly owned, or subject to an obligation of common

In this case, the prior art qualifies under 102(a) as well as 102(e) and therefore cannot be disqualified as commonly owned.

As regards Knepp et al, applicants' arguments are convincing. However, given the above arguments, the 103 rejection stands.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARIA B. MARVICH whose telephone number is (571)272-0774. The examiner can normally be reached on M-F (7:00-4:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, PhD can be reached on (571)-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Maria B Marvich, PhD
Primary Examiner
Art Unit 1633

/Maria B Marvich/
Primary Examiner, Art Unit 1633